DOCKET NO: 281760US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:	
ANGELO GUGLIELMOTTI, ET AL.	:	EXAMINER: RAMACHANDRAN, U.
SERIAL NO: 10/560,836	:	
FILED: MARCH 30, 2006	:	GROUP ART UNIT: 1617
FOR: USE OF 2H-[1,3]-OXAZINO [3, 2-A] INDOLE DERIVATIVES FOR THE TREATMENT OF NEUROPATHIC PAIN	:	

REPLY BRIEF

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

In response to the Examiner's Answer mailed August 7, 2008, the Appellants respectfully ask for reversal of the rejections on appeal based on the arguments in the Appeal Brief and in this Reply Brief.

Reply to Examiner's Arguments with Respect to Grounds of Rejection on Appeal

In addition to the arguments in the Appeal Brief regarding the obviousness rejections of issues (A)-(D), the Appellants respectfully bring the Board's attention to the following points. First, the Examiner attempts to make the connections between the several references relied upon by using the present application as a guide, that is by employing a hindsight approach to attempt to piece together a rationale for combining disparate teachings regarding 5-HT4 antagonist of Gaster, et al. and treatment of irritable bowel syndrome and migraine with those of Smith regarding use of the combination of 5-HT4 antagonists and 5-HT3 antagonists to treat intestinal allodynia. The Examiner conflates intestinal allydynia with allodynia associated with neuropathic pain by reference to Jorum. However, Jorum is silent with respect to the effects of the compound of formula (I) on neuropathic pain, as are both Gaster and Smith. The missing link in the Examiner's argument any nexus in the prior art that the pain disorders described by Gaster and Smith are mediated by the same mechanism as those responsible for causing neuropathic pain, and that the mechanism causing neuropathic pain is targeted by the compound of formula (I).

Second, in using such a hindsight approach, the Examiner has wrongly assumed that the treatment of a clinical finding that allodynia or hyperalgesia inevitably lead a man skilled in the art to suppose that any type of pain can be treated. It is worth noting that the Examiner employs the terms like "hallmark" or "clinical feature" in a way suggesting that allodynia is a distinctive character of neuropathic pain. Further, the Examiner asserts that "migraine is linked to neuropathic pain via the clinical feature allodynia. Hence, by treating migraine attacks in patients allodynia is treated and in turn

the neuropathic pain" (see page 11, last seven lines, page 12, last two lines of 1st paragraph, and page 13, 2nd paragraph, last five lines). These statements are simply not true.

Both allodynia and hyperalgesia are generic clinical findings of different pathologic states having different origins like, for example, rheumatoid arthritis, which is due to an erosion and damage of the bone and cartilage tissues, migraine, which is mainly due to a vasodilatation and pulsation of the cephalic vessels, intestinal colic, which is due to hypermotility and extension and intestinal walls, and finally, neuropathic pain, which is due to primary lesions or dysfunctions of the nervous system. The prior art does not provide a reasonable expectation that pain, including allodynia or hyperalgesia, associated with radically different disorders having different etiologies and pathological manifestations, could be treated with the same compound. So, what was true, was that a man of ordinary skill in the art was aware that each pathologic state and disorder required a specific treatment, and that there was no reasonable expectation of success that a treatment able to mitigate migraine and its associated allodynia and/or hyperalgesia would have also able to mitigate rheumatoid arthritis and/or intestinal colic and/or neuropathic pain.

As a paradox, if the reasoning of the Examiner was true, it would have been enough to have one analgesic compound for alleviating all the pains of the world. Unfortunately, this is not the case, and the scientific and pharmaceutical research is always searching for new compounds, each tailored for a specific kind of pain.

In view of the arguments presented in the Appeal Brief and in this Reply Brief, the Appellants respectfully submit that obviousness rejections on appeal cannot be sustained.

RELIEF REQUESTED

The Appellants respectfully request that grounds of rejection (A)-(D) be REVERSED.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Customer Number
22850

Thomas M. Cunningham
Registration No: 45,394